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Heller Ehrman & McAuliffe
Suite 300
1666 K Street Northwest
Washington, DC 20006

EXAMINER.

FETTEROLF, BRANDON J

ART UNIT

PAPER NUMBER

1642

DATE MAILED: 01/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/734,589	Applicant(s) GOVINDAN, SERENGULAM V.	
	Examiner Brandon J. Fetterolf, PhD	Art Unit 1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 October 2005.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-62 is/are pending in the application.
- 4a) Of the above claim(s) 5-8 and 51-62 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4 and 9-50 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input checked="" type="checkbox"/> Other: <u>See Continuation Sheet.</u> |

Continuation of Attachment(s) 6). Other: Definitions for Small Cell Lung cancer and Parenteral.

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Govindan et al.

DETAILED ACTION

Election/Restrictions

The Election filed on October 20, 2005 in response to the Restriction Requirement of September 21, 2005 has been entered. Applicant's election of Group I, claims 1-4 and 9-50, as specifically drawn to an immunoconjugate comprising a targeting moiety, a chemotherapeutic moiety and a linker binding to the targeting moiety via a thiol group, and to the chemotherapeutic moiety via an intracellularly-cleavable moiety, wherein the intracellular moiety is an ester moiety has been acknowledged.

Applicant's election with traverse of Group I, claims 1-4 and 9-50 are acknowledged. However, because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the restriction requirement is deemed to be proper and is made FINAL.

Claims 1-62 are currently pending.

Claims 5-8 and 51-62 have been withdrawn from consideration as being drawn to a non-elected invention.

Claims 1-4 and 9-50 are currently under consideration.

Species Election

Acknowledgement is made of Applicants election of the following species:

- N,N'-dialkyl substituted piperazine from claims 14 and 31.
- SN-38 from claims 15 and 34.
- CD22 from claims 24 and 43.
- LL2 from claims 26 and 47.

Upon further review and reconsideration, the examiner has withdrawn the species election.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 32 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In the instant case, the formula shown in claim 32 renders the claim indefinite because the neither the specification or the claims appear to identify what “R” could be.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4, 9-15, 27-34 and 48-50 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In the instant case, the claims are inclusive of a genus of targeting moieties. However, the written description in this case only sets forth one species of targeting moieties, wherein the targeting moiety is an antibody.

The specification teaches (page 11, paragraph 004) that the preferred targeting moiety of the invention include, but is not limited to, antibodies, antibody fragments and binding proteins incorporation sequences from antibodies or antibody fragments. Moreover, the specification teaches monoclonal antibody conjugates comprising monoclonal antibodies as the targeting moiety linked to CPT-11 as the chemotherapeutic agent (page 26, Example 5 to page 28, Example 7). In the instant case, those of skill in the art recognize that the term “targeting moiety” refers to a genus of molecules which bind to a biological target. For example, Danthi et al. (US 2003/0133972 A1, 2003) teaches that the term “targeting entities” includes, but are not limited to, antibodies, receptor-

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binding ligands, molecules that bind to enzymes, nucleic acids or aptamers and one or more members of a specific binding interaction such as biotin or iminobiotin and avidin or streptavidin (page 15, paragraph 0148). Thus, in view of the prior art's interpretation of the term "targeting moiety", the specification only reasonably conveys one species of targeting moieties (i.e., antibodies); and therefore, is not commensurate with the full scope of any and/or all targeting moieties. A description of a genus may be achieved by means of a recitation of a representative number of species falling within the scope of the genus or by describing structural features common the genus that "constitute a substantial portion of the genus." See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997): "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cNDA, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus."

The court has since clarified that this standard applies to compounds other than cDNAs. See University of Rochester v. G.D. Searle & Co., Inc., ___F.3d___, 2004 WL 260813, at *9 (Fed.Cir.Feb. 13, 2004). The instant specification fails to provide sufficient descriptive information, such as definitive structural or functional features that are common to the genus. That is, the specification provides neither a representative number of molecules that encompass the genus of targeting moieties nor does it provide a description of structural features that are common to the molecules. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, the disclosure of one species of targeting moieties is insufficient to describe the genus. Thus, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe and enable the genus as broadly claimed.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure(s) of the encompassed genus of targeting moieties, and therefore conception is not achieved until reduction

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to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only one species of targeting moieties, wherein the targeting moiety is an antibody, but not the full breadth of the claims, meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 9-10, 16-17, 21-22, 24 and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by Abrams et al. (US 5,112,954, 1992).

Abrams et al. teach (column 5, lines 38-40) an immunoconjugate comprising a targeting entity attached to a cytotoxic agents, wherein the targeting entities include, but are not limited to, hormones or antibodies. With regards to the antibodies, the patent teaches (column 5, lines 45-64) that the antibodies may be genetically engineered antibodies or intact monoclonal antibodies and/or functional fragments thereof, wherein the monoclonal antibodies are specific for a tumor-associated antigen in humans such as, anti-TAC or other interleukin 2 receptor antibodies, NR-ML-05 (specific for melanoma) and NR-LU-10 (specific for pancarcinoma). The patent further teaches (page 7, lines 41-66) that the targeting entity and cytotoxic agent are attached via a linker, wherein a free thiol

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group present on the targeting entity may be reacted with an activated double bond (e.g., the double bond of a maleimido group on a linker) to produce a thioether bond. Moreover, Abrams et al. teach (column 8, lines 28-36) that the immunoconjugates comprising linkages are cleavable in the vicinity of the target site such that the agent is delivered and released at the specific target site. For example, the patent teaches (column 11, lines 23-40 and column 23-54) that the immunoconjugate may be cleaved at the ester moiety intracellularly via an esterase.

Claims 1-4, 9, 11, 16-17, 19, 21-23, 27-29, 33, 35-36, 38, 40-42 and 48-49 are rejected under 35 U.S.C. 102(b) as being anticipated by Chari et al. (WO 01/24763 A2, 2001).

Chari et al teach (page 2, lines 11-14 and page 5, lines 30-31) an immunoconjugate comprising a cell binding agent and at least one therapeutic agent for killing a selected cell population, wherein the cell binding agent is a monoclonal antibody or fragment thereof (i.e. Fv, Fab, Fab' and F(ab')₂) and the therapeutic agent is an anti-mitotic agent that is linked to the antibody via a linking group. With regards to the antibody, the WO publication teaches (page 17, lines 3-5) that the choice of the appropriate antibody depends on the cell population that is to be targeted. For example, Chari et al. teach (page 17, lines 6-13) that the monoclonal antibody anti-B4 which is a murine IgG1, that binds to the CD19 antigen on B cells can be used to target B cells. Alternatively, the WO publication teaches (page 17, lines 23-31) that antibody or fragment thereof that is specific for lung cancer such as an antibody that binds to an epitope on the CD56 antigen expressed on small cell lung cancers. With regards to the linking group, Chari et al. teach (page 6, lines 1-2) that suitable linking groups include, but are not limited to, esterase labile groups. Moreover, the WO publication teaches (page 6, lines 4-14, page 7, lines 1-5, page 9, formula II and/or III and page 21, lines 28-30) that the linking group is part of a chemical moiety having a peptide such as N-methyl-cysteine or N-methyl-alanine, covalently bound at the C-terminus to an anti-mitotic agent, such as a maytansinoid derivative, via an ester linkage and at the N-terminus to the cell-binding agent, i.e., antibody, via a reactive thiol group, wherein the antibody has been modified with a maleimido group. As a result, the WO publication teaches (page 22, lines 1-2) the conjugates would have 1 to 10 drug molecules per antibody molecule. Moreover, Chari et al. teach (page 30, lines 9-22) that the immunoconjugates may be administered in a suitable form via i.v.. Thus, while Chari et al. do not characterize an antibody specific for an antigen expressed on small cell lung cancer as an antibody

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specific for an antigen expressed on a carcinoma cell, the claimed functional limitation would be an inherent property because as evidenced by Dictionary.com (see attached), small cell lung cancer is also referred to as small-cell lung carcinoma. Moreover, although Chari et al. does not specifically recite that the immunoconjugate is formulated for parental administration, the claimed functional limitation would be an inherent property because as evidenced by Stedman's Medical Dictionary (see attached), the term parental refers to the introduction of substances to an organism by intravenous, subcutaneous, intramuscular, or intramedullary injection. Thus, the claimed immunoconjugate appears to be the same as the prior art. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See *In re Best* 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte Gray* 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 15 and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chari et al. (WO 01/24763 A2, 2001) in further view of Voegelien et al. (J. Med. Chem. 1991; 34: 992-998) or Bennouna et al. (Int. J. Clin. Oncol. 2002; 7: 236-244) or Perez et al. (European Journal of Pharmacology 1998; 356: 239-243).

Chari et al teach, as applied to claims 1-4, 9, 11, 16-17, 19, 21-23, 27-29, 33, 35-36, 38, 40-42 and 48-49 above, an immunoconjugate comprising a cell binding agent and at least one therapeutic agent for killing a selected cell population, wherein the cell binding agent is a monoclonal antibody or fragment thereof and the therapeutic agent is an anti-mitotic agent that is linked to the antibody

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via a linking group (page 2, lines 11-14 and page 5, lines 30-31). With regards to the anti-mitotic agent, the WO publication teaches (page 4, lines 25-30) that any anti-mitotic agent known in the art can be used such as maytansinoids, Vinca alkaloids, dolastatins, or cryptophycins..

Chari et al. do not explicitly teach that the anti-mitotic agent is a taxane, doxorubicin and/or analog thereof, or camptothecin, e.g. CPT, and/or analog thereof.

Voegelien et al. teach that taxol derivatives possess antimitotic activity.

Bennouna et al. teach (page 236, 1st column, 3rd paragraph) that irinotecan (CPT-11) is an antimitotic agent.

Perez et al. teach (abstract) that doxorubicin is an anti-mitotic agent.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to substitute equivalents known for the same purposes in view of the teachings of the references. One would have been motivated to do so because each of the agents, e.g. taxol, irinotecan and CPT-11 have been individually taught in the prior art to be anti-mitotic agents. The instant situation is amenable to the type of analysis set forth in Smith v. Hayashi, 209 USPQ 754 (Bd. of Pat. Inter. 1980) wherein the court found that “[T]he mere fact that phthalocyanine and selenium function as equivalent photoconductors in the claimed environment was not sufficient to establish that one would have been obvious over the other. However, there was evidence that both phthalocyanine and selenium were known photoconductors in the art of electrophotography. “This, in our view, presents strong evidence of obviousness in substituting one for the other in an electrophotographic environment as a photoconductor.” 209 USPQ at 759. Applying the same logic to the instant claims, one of ordinary skill in the art would have a reasonable expectation of success that by substituting art recognized anti-mitotic agents such as taxol, irinotecan or doxorubicin for the anti-mitotic agents taught by Chari et al., one would achieve an anti-mitotic immunoconjugate.

Claims 12-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chari et al. (WO 01/24763 A2, 2001) in combination with Voegelien et al. (J. Med. Chem. 1991; 34: 992-998) or Bennouna et al. (Int. J. Clin. Oncol. 2002; 7: 236-244) or Perez et al. (European Journal of Pharmacology 1998; 356: 239-243) in further view of Li et al. (2001/0034363, 2001) and Miller et al. (224th ACS National Meeting, August 18-22, 2002, Boston, Mass., Poster Presentation).

The combination of Chari et al with Voegelien et al. or Bennouna et al. or Perez et al. teach, as applied to claims 1-4, 9, 11, 15-17, 19, 21-23, 27-29, 33-36, 38, 40-42 and 48-49 above, an immunoconjugate comprising a cell binding agent and at least one therapeutic agent for killing a selected cell population, wherein the cell binding agent is a monoclonal antibody or fragment thereof and the therapeutic agent is an anti-mitotic agent, such as a taxol, irinotecan or CPT-11, that is linked to the antibody via a linking group.

The combination of Chari et al with Voegelien et al. or Bennouna et al. or Perez et al. does not explicitly teach that the linker further comprises a water-solubilizing moiety between the therapeutic moiety and the cell binding agent, wherein the water-solubilizing agent is an aminopolycarboxylate such as DPTA, DOTA, EDTA and TETA.

Li et al. teach (page 1, paragraph 0003) that the major difficulty in the development of paclitaxel for clinical trial use has been its insolubility in water. As a result, the publication teaches a water-soluble paclitaxel derivatives. Specifically, Li et al. teach (page 2, paragraph 0016 and page 3, paragraph 0017) paclitaxel conjugated to a water-soluble metal chelator such as DPTA, DOTA, EDTA and TETA. In addition, the publication teaches (page 2, paragraph 0012) that other therapeutic agent such as doxorubicin and camptothecin may be conjugated to water-soluble moieties.

Miller et al. teach the development of Taxoid derivatives with enhanced toxicity and solubility. Specifically, the poster teaches (2nd column, IV. Attempts to Improve Water Solubility) that one problem associated with antibody-drug conjugate formation is the presence of free drug found in the conjugate as a result of hydrophobic interactions that the cause the drug to “stick” to the antibody such that it compromises the efficiency of the antibody.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to incorporate a water soluble moiety into the immunoconjugate taught by the combination of Chari et al with Voegelien et al. or Bennouna et al. or Perez et al. in view of the teachings of Li et al.. One would have been motivated to do so because as taught by Miller et al., one problem associated with antibody-drug conjugate formation is the presence of free drug found in the conjugate as a result of hydrophobic interactions that the cause the drug to “stick” to the antibody such that it compromises the efficiency of the antibody. Thus, one of ordinary skill in the art would have a reasonable expectation of success that by incorporating a water soluble moiety into

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the immunoconjugate taught by the combination of Chari et al with Voegelien et al. or Bennouna et al. or Perez et al. in view of the teachings of Li et al., one would achieve a way of overcoming poor water solubility and increasing the antibodies efficiency.

Claims 25 and 44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chari et al. (WO 01/24763 A2, 2001) in view Newton et al. (Blood 2001; 97: 528-535).

Chari et al teach, as applied to claims 1-4, 9, 11, 16-17, 19, 21-23, 27-29, 33, 35-36, 38, 40-42 and 48-49 above, an immunoconjugate comprising a cell binding agent and at least one therapeutic agent for killing a selected cell population, wherein the cell binding agent is a monoclonal antibody or fragment thereof (i.e. Fv, Fab, Fab' and F(ab')₂) and the therapeutic agent is an anti-mitotic agent that is linked to the antibody via a linking group. With regards to the antibody, the WO publication teaches (page 17, lines 3-5) that the choice of the appropriate antibody depends on the cell population that is to be targeted. For example, Chari et al. teach (page 17, lines 6-13) that the monoclonal antibody anti-B4 which is a murine IgG1, that binds to the CD19 antigen on B cells can be used to target B cells. Alternatively, the WO publication teaches (page 17, lines 23-31) that antibody or fragment thereof that is specific for lung cancer such as an antibody that binds to an epitope on the CD56 antigen expressed on small cell lung cancers.

Chari et al. does not explicitly teach that the targeting moiety is the antibody LL2.

Newton et al. teach (abstract) an immunoconjugate comprising LL2 covalently linked to the ribonuclease, onconase, wherein LL2 is an anti-CD22 monoclonal antibody against B-cell lymphoma.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to combine the immunoconjugate as taught by Chari et al. with a monoclonal LL2 antibody in view of the teachings of Newton et al.. One would have been motivated to do so because as taught by Newton et al., the murine anti-CD22 monoclonal antibody (LL2) was developed for imaging and treatment of non-Hodgkin B-cell lymphomas (NHL). Thus, one of ordinary skill in the art would have a reasonable expectation of success that by incorporating LL2 into the immunoconjugate of Chari in view of the teachings of Newton, one would achieve an immunoconjugate which comprises a targeting agent specific for Non-Hodgkin B-cell lymphomas.

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Claims 18, 20, 26, 37, 39, 45 and 47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chari et al. (WO 01/24763 A2, 2001) combined with Newton et al. (Blood 2001; 97: 528-535) in view of Cao et al. (Bioconjugate Chemistry 1998; 9: 635-643).

Chari et al. combined with Newton et al. teach, as applied to claims 1-4, 9, 11, 16-17, 19, 21-23, 25, 27-29, 33, 35-36, 38, 40-42, 44 and 48-49 above, an immunoconjugate comprising a cell binding agent and at least one therapeutic agent for killing a selected cell population, wherein the cell binding agent is a monoclonal antibody or fragment thereof (i.e. Fv, Fab, Fab' and F(ab')₂) and the therapeutic agent is an anti-mitotic agent that is linked to the antibody via a linking group. Specifically, the combination teaches that the cell binding agent is the monoclonal antibody LL2.

Chari et al. combined with Newton et al. do not explicitly teach that the antibody and/or specifically LL2 is multispecific and/or bispecific.

Cao et al. teaches (page 640, 1st column, 2nd full paragraph) that bsMAb's (bispecific monoclonal antibodies) can be used as an effective delivery system for cancer treatment. Specifically, the reference teaches (page 640, 1st column, 3rd full paragraph) that the advantages of using bsMAb to deliver high molecular weight toxins or drugs to tumors, compared to conjugating such moieties to a Mab, is that chemical conjugations are totally avoided which provides for a more uniform cross-linking between the target and the effector molecule.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use a bispecific antibody as the cell-binding agent of the immunoconjugate in view of the teachings of Cao et al.. One would have been motivated to do so because as taught by Cao et al., the advantages of using bsMAb to deliver high molecular weight toxins or drugs to tumors, compared to conjugating such moieties to a Mab, is that chemical conjugations are totally avoided which provides for a more uniform cross-linking between the target and the effector molecule. Thus, one of ordinary skill in the art would have a reasonable expectation of success that by using a bispecific antibody as the cell-binding agent of the immunoconjugate taught by Chari et al., one would achieve an immunoconjugate which provides a more uniform cross-linking between the target and the drug molecule.

Therefore, NO claim is allowed.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brandon J. Fetterolf, PhD whose telephone number is (571)-272-2919. The examiner can normally be reached on Monday through Friday from 8:30 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeff Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Brandon J Fetterolf, PhD
Examiner
Art Unit 1642

BF

A handwritten signature in black ink, appearing to read "Gary B. Nickol". The signature is written in a cursive, flowing style.

GARY B. NICKOL, PH.D.
PRIMARY EXAMINER